July 9, 2009

Dr. Barbara Shane
Executive Secretary
Office of Chemical Nomination and Selection
National Toxicology Program (NTP),
National Institute of Environmental Health Sciences (NIEHS)
National Institutes of Health (NIH)
U.S. Department of Health and Human Services (HHS)
P.O. Box 12233
MD A3-07
Research Triangle Park, NC 27709

Re: Comments on the Chemical Information Review Document for Deoxynivalenol (CAS No. 51481-10-8)

Dear Dr. Shane:

The Grocery Manufacturers Association (GMA) represents the world's leading food, beverage and consumer products companies. The association promotes sound public policy, champions initiatives that increase productivity and growth and helps to protect the safety and security of the food supply through scientific excellence. The GMA board of directors is comprised of chief executive officers from the Association's member companies. The $2.1 trillion food, beverage and consumer packaged goods industry employs 14 million workers and contributes over $1 trillion in added value to the nation's economy.

GMA appreciates the opportunity to submit these comments on the nomination of deoxynivalenol for toxicological evaluation by NTP/NIEHS.[1] Deoxynivalenol (DON) is among the class of type B-tricothecene mycotoxins produced by certain *Fusarium* fungal species. Commodities commonly infected are cereal crops (the major ones being wheat, corn and barley) and processed grains (e.g., malt, beer, and bread). NTP/NIEHS nominated DON for evaluation of chronic toxicity and carcinogenicity studies and reproductive toxicity studies. NTP purports that definitive long-term studies are lacking.

[1] 74 FR 25241 [May 27, 2009], http://edocket.access.gpo.gov/2009/pdf/E9-12204.pdf

GMA believes that NTP's resources would be better directed to studying chemicals that are not presently being adequately addressed, and requests that NTP give DON a very low priority for testing, for the following reasons.

- The potential public health impacts of DON and other *Fusarium* toxins have been recognized for many years. There are some areas of the world where their presence is endemic or cyclic, causing human illness. Accordingly, these naturally-occurring compounds are the focus of ongoing regulatory and risk management attention globally.
- DON is the most extensively studied tricothecene. Abundant data exist, and, based on review and expert evaluation by worldwide food regulatory and scientific bodies, have been determined to be sufficient for tolerable daily intake levels and regulatory limits and/or guidance to be established. We discuss this in more detail below. Additional testing is unlikely to make a significant new contribution to understanding and managing public health risks from DON.
- Government researchers, grain producers and handlers, the milling industry and food processors are actively engaged in monitoring, management practices and research to control exposures from contaminated grains.

Expert Evaluations of DON

It is important to note that natural contamination is very often a mixture of trichothecenes that that can differ with geography and over time, so the toxicology data gaps that have been identified as important for protection of public health focus on the family of toxins, and understanding whether significant differences in toxicity or metabolism exist between compounds and species, including animals used for food.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated DON thoroughly in 2001.[2] JECFA found the data sufficient to set a provisional maximum tolerable daily intake (PMTDI) of 1 μg/kg bw, based on the No Observed Effect Level related to decreased weight gain, the most sensitive effect. JECFA concluded that DON did not present a carcinogenic hazard based on a long-term rodent study, and that intake at levels similar to the PMTDI would not result in effects of DON on the immune system, growth, or reproduction. The only insufficiency in the available toxicology data that JECFA noted was acute toxicity of DON.

JECFA will revisit DON in light of new information at its 72nd meeting in February 2010.[3] They will specifically consider the need for an acute Reference Dose. Toxicity of DON and its acetyl-derivatives will be considered.

The European Commission Scientific Committee on Food (SCF) evaluated *Fusarium* toxins individually and as a group and has published several Opinions (Part 1 – Part 6). The toxicological review of DON was based on the Dutch evaluation of DON (1999) and

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[2] http://www.inchem.org/documents/jecfa/jecmono/v47je05.htm)
[3] http://www.who.int/ipcs/food/jecfa/jecfa72.pdf

on the report "Fusarium toxins in cereals – a risk assessment" (1998) prepared for the Nordic Council of Ministers. The individual evaluations resulted in temporary Tolerable Daily Intake (TDI) levels for the various toxins including DON.[4] However, once the toxicity data available for the group as a whole was considered, the information was deemed sufficient to establish a full TDI for DON that was considered protective of public health at 1 μg/kg bw.[5]

In a 2002 Opinion that considered the group evaluation of T-2 toxin, HT-2 toxin, nivalenol, and DON, SCF noted that the available information on DON was sufficient to remove the temporary-TDI previously set and replace it with a full TDI. The Committee noted that synergism has not been observed between DON and the other tricothecenes evaluated. [6]

Regulation of DON

Exposures to DON in the US and Europe are episodic and relatively infrequent, as outbreaks are associated with climatic factors. Nevertheless, levels of DON are regulated. There are FDA advisory levels of 1 ppm in finished wheat products for human consumption, as well as limits for grain and byproducts used in poultry, swine and cattle feed.[7] European Commission Regulation EC 1881/2006 set maximum limits for DON in unprocessed cereals, durum, wheat, maize (not including rice) and processed cereal, dry pasta, bread, processed cereal-based foods (e.g., baby foods). [8] Commission Regulation EC /2007 amends Regulation EC 1881/2006 as to permitted maximum levels of DON in raw commodities as well as in finished products.[9]

In summary, GMA submits that DON does not meet any of NTP's principles for further evaluation of a chemical. DON should be rejected as a candidate for testing, or given the lowest possible priority, so that NTP resources can be directed where they can better serve public health.

Sincerely,

[Redacted]

Robert E. Brackett, Ph.D.
Senior Vice President and Chief Science and Regulatory Officer
Grocery Manufacturers Association

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[4] http://ec.europa.eu/food/fs/sc/scf/out44_en.pdf
[5] http://ec.europa.eu/food/fs/sc/scf/out123_en.pdf
[6] http://ec.europa.eu/food/fs/sc/scf/out123_en.pdf
[7] http://www.gipsa.usda.gov/GIPSA/documents/GIPSA_Documents/b-vomitox.pdf
[8] http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_364/l_36420061220en00050024.pdf
[9] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:255:0014:0017:EN:PDF